Neutrokine- α

1	AAATTCAGGATAACTCTCCTGAGGGGTGAGCCCAAGCCCTGCCATGTAGTGCACGCAGGAC	60
61	ATCAACAACACAGATAACAGGAAATGATCCATTCCCTGTGGTCACTTATTCTAAAGĞCC	120
l21 1	CCAACCTTCAAAGTTCAAGTAGTGATATGGATGACTCCACAGAAAGGGAGCAGTCACGCC M D D S T E R E Q S R L	180 12
181 13	TTACTTCTTGCCTTAAGAAAAGAGAAGAAATGAAACTGAAGGAGTGTGTTTCCATCCTCC T S C L K K R E E M K L K E C V S I <u>L P</u> CD-I	240 32
241 33	CACGGAAGGAAAGCCCCTCTGTCCGATCCTCCAAAGACGGAAAGCTGCTGGCTG	300 52
301 53	TGCTGCTGGCACTGCTGCTTGCTGCCTCACGGTGGTGTCTTTCTACCAGGTGGCCGCCC L L A L L S C C L T V V S F Y Q V A A L	360 72
361 73	TGCAAGGGACCTGGCCAGCCTCCGGGCAGAGCTGCAGGGCCACCACGCGGAGAAGCTGC Q G D L A S L R A E L Q G H H A E K L P CD-II	420 92
121 93	CAGCAGGAGCAGGAGCCCCCAAGGCCGGCCTGGAGGAAGCTCCAGCTGTCACCGCGGGAC A G A G A P K A G L E E A P A V T A G L CD-III #	480 112
181 113	TGAAAATCTTTGAACCACCAGCTCCAGGAGAAGGCAACTCCAGTCAGAACAGCAGAAATA K I F E P P A P G E G N S S Q N S R N K	540 132
541 133	AGCGTGCCGTTCAGGGTCCAGAAGAAACAGTCACTCAAGACTGCTTGCAACTGATTGCAG R A V Q G P E E T V T Q D C L Q L I A D CD-IV	600 152

FIG.1A

Neutrokine- α

601 153	ACAGTGAAACACCAACTATACAAAAAGGATCTTACACATTTGTTCCATGGCTTCTCAGCT S E T P T I Q K G S Y T F <u>V P W L L S F</u> CD-V	660 172
661 173	TTAAAAGGGGAAGTGCCCTAGAAGAAAAAGAGAAATATTGGTCAAAGAAACTGGTT K R G S A L E E K E N K I L V K E T G Y CD-VI CD-VI	720 192
721 193	ACTITITATATATGGTCAGGTTITATATACTGATAAGACCTACGCCATGGGACATCTAA FFIYGQVLYTDKTYAMGHLI CD-VI CD-VII	780 212
781 213	TTCAGAGGAAGAAGGTCCATGTCTTTGGGGATGAATTGAGTCTGGTGACTTTGTTTCGAT Q R K K V H V F G D E L S L V T L F R C CD-VII	840 232
841 233	GTATTCAAAATATGCCTGAAACACTACCCAATAATTCCTGCTATTCAGCTGGCATTGCAA I Q N M P E T L P N N <u>S C Y S A G</u> I A K CD-VIII CD-IX	900 252
901 253	AACTGGAAGAAGGAGATGAACTCCAACTTGCAATACCAAGAGAAAATGCACAAATATCAC <u>L E E G D E L Q L A I P R</u> E N A Q I S L CD-X	960 272
961 273	TGGATGGAGATGTCACATTTTTTGGTGCATTGAAACTGCTGTGACCTACTTACACCATGT D G D V <u>T F F G A L K L</u> L CD-XI	1020 285
1021	CTGTAGCTATTTTCCTCCCTTTCTCTGTACCTCTAAGAAGAAAGA	1080
1081	CCAAAAAAAAAAAAAA 1100	

FIG.1B

		11 mg
TNFalpha TNFbeta LTbeta FasLigand Neutrokine alpha	TNFalpha TNFbeta LTbeta FasLigand Neutrokine alpha	TNFalpha TNFbeta LTbeta FasLigand Neutrokine alpha
10 M S T E S M I R D V E L A E E A M T P P E R L M G A T P P E R L M Q Q P F N Y P Y P Q I Y W - V D S S A S S P W A P P G T V M D D S T E R E Q S R L T S C L K K R E E M K L K E C V S I	40 50 60 60 60 60 60 60 60 60 60 60 60 60 60	70 80 90 90 90 90 90 90 90 90 90 90 90 90 90
	17 8 8 4 4 31 31 31	30 9 12 60 60 58

FIG.2A

a I pha	alpha	alpha
a I pha SV	alphaSV	alphaSV
TNFalpha	TNFalpha	TNFalpha
TNFbeta	TNFbeta	TNFbeta
LTbeta	LTbeta	LTbeta
FasLigand	FasLigand	FasLigand
Neutrokine al	Neutrokine	Neutrokine alpha
100 110 120 31 GAQGLPGATTLFCLLHFGVIGPQREEFPR 32 LLLMVPITVLAVLALVPQDQGLVTETADP 90 VLVALVGLGLGMFQLFHLQKELAELRESTS 88 AEKLPAGAGAPKAGLEEAPAVTAGLKIFEP 88 AEKLPAGAGAPKAGLEEAPAVTAGLKIFEP 130 140 150	- Q A V R S S S R T P S D K P V - T A R Q H P K M H L A H S T L K P A F Q K L P E E P E T D L S P G L P A F Q K Q I G H P S P P P E K K E L R K V N S R N K R A V Q G P E E T V T Q D C N S R N K R A V Q G P E E T	160 170 180 66 H L I G D P S K Q N - S L Q W L N R R A N A L L 91 H L I G A P L K - G Q G L G W E T I K E Q A F L 148 H L T G K S N S R S M P L E W E D I Y G I V L L 148 Q L I A D S E T P T I Q K G S Y T F V P W L L S F K 142 G S Y T F V P W L L S F K

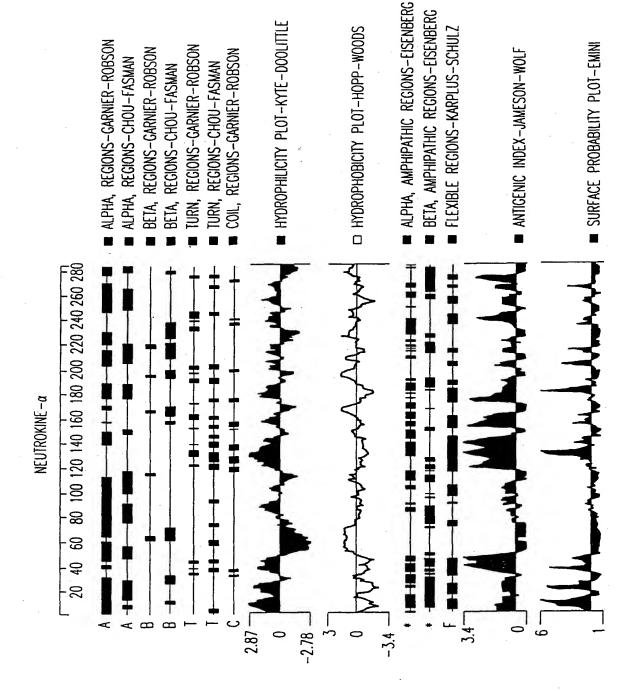
. 57

FIG.2B

		1. 6.3824
TNFalpha TNFbeta LTbeta FasLigand Neutrokine alpha Neutrokine alphaSV	TNFalpha TNFbeta LTbeta FasLigand Neutrokine alpha Neutrokine alphaSV	TNFalpha TNFbeta LTbeta FasLigand Neutrokine alpha Neutrokine alphaSV
114 A N G V E L R D N - Q L V V P S E G L Y L I Y S Q V L F K G S Q V R S G V R S G V R S G V R S G V R S G V R S G V R S G V V R S G V V R S G V V R S G V V R S G V V R S G V V R S G V V R R G S A L E E K E N K I L V K E T G Y F F I Y G Q V L Y T D I S G R G S A L E E K E N K I L V K E T G Y F F I Y G Q V L Y T D I S G S A L E E K E N K I L V K E T G Y F F I Y G Q V L Y T D I S G S A L E E K E N K I L V K E T G Y F F I Y G Q V L Y T D I S G S A L E E K E N K I L V K E T G Y F F I Y G Q V L Y T D	220 230 240 143 Q G C P S T H V L L T H T I S R I A V S Y Q T K 118 K A Y S P K A T S S P L Y L A H E V Q L F S Q Y P F H 144 R A P P G G D P Q G R S V T L R S S L Y R A G G A Y G P G 200 Q S C N N L P L S H K V Y M R N S K Y P Q D 204 K T Y A M G H L I Q R K K V H V F G D E L S 185 K T Y A M G H L I Q R K K V H V F G D E L S	250 260 270 167 VN L L S A I K S P C Q R E T P E G A E A K P W Y E 146 V P L L S S Q K W V Y P G L Q E P W L H 174 T P E L L L E G A E T V T P V L D P A R R Q G Y G P L W Y T 222 L V M M E G K M M S Y C T T G Q M W A R 226 L V T L F R C I Q N M P E T L P N T T G Q M W A R 207 L V T L F R C I Q N M P E T L P N I N FIG. 2 C
$-\omega$		

TNFalpha	TNFalpha
TNFbeta	TNFbeta
LTbeta	LTbeta
FasLigand	FasLigand
Neutrokine alpha	Neutrokine alpha
290 300 EKGDRLSAEINRPDYLDFAE TQGDQLSTHTDGIPHLVLSP RRGERVYWNISHPDMVDFAR TSADHLTWNVSELSLWNFEE EGDELQLAIPRENAQISLD	9 7
280	310
166 S M Y H G G V F Q L E K G D R I	196 S - T V F G I I A
204 S V G F G G L V Q L R R G E R V	234 - G K T F F G A F A
242 S S Y L G A V F N L T S A D H I	272 S - Q T F F G L Y K
244 S C Y S A G I A K L E E G D E I	274 G D V T F F G A L K
225 S C Y S A G I A K L E E G D E	255 G D V T F F G A L K

FIG.2D



0

	1				50
HSOAD55R HNEDU15X		GGATAACTC	T CCTGAGGGGT	GAGCCAAGC	C CTGCCATGTA
HSLAH84R HLTBM08R	AATTCGGCAC	GAGCAAGGC	GGCCTGGAGG	TATATATGG AAGCTCCAG	CAGGTTTTAT CTGTCACCGCG
HSOAD55R HNEDU15X HSLAH84R	GTGCACGCAG	GACATCAACA	A ACACAGA	TAACAGGAA	100 TAÂTCCATTC TGATCCATTC GGAAGAAGGTC
HLTBM08R	GGACTGAAAA	TCTTTGAACC	ACCAGCTCCA	GGAGAAGGCA	ACTCCAGTCA
HSOAD55R HNEDU15X HSLAH84R HLTBM08R	CCTGTGGTCA CATGTCTTTG	CTTATTCTAA GGGATGAATT	AGGCCCCAAC GAGTCTGGTG	CTTCAAAGTT	150 CAAGTAGTGA CAAGTAGTGA GATGTATTCA ACAGTCACTC
HSOAD55R HNEDU15X HSLAH84R HLTBM08R	TATGGATGAC AAATATGCCT	TCCACAGAAA GAAACACTAC	GGGAGCAGTC CCAATAATTC	ACGCCTTACT CTGCTATTCA	200 TCTTGCCTTA TCTTGCCTTA GCTGGCATTG TATACAAAAA
HSOAD55R HNEDU15X HSLAH84R HLTBM08R	AGAAAAGAGA CAAAACTGGN	AGAAATGAAA AGGAAGGA	CTGNAAGGAG CT.GAAGGAG GATGAAC TTTGGGCCAA	TGTGTTTCCA TCCAACTTGC	TCCTCCCACG AATACCAGGG
HSOAD55R HNEDU15X HSLAH84R HLTBM08R	GAAGGAAAGC GAAAATGCAC	CCCTCTGTCC AATTATCACT	GATCCTCCAA GATCCTCCAA GGGATGGAGA CTCTTCAGAT	AGACGGAAAG TGTTCACATT	CTGCTGGCTG TTTTGGGTGC
HSOAD55R HNEDU15X HSLAH84R HLTBM08R	301 CAACCTTGNT CAACCTTGCT CATTGAAACT CAAAGGAAAA	GCTGGCACTG GCTGTGACCT	CTGTCTTGCT NCTTACANCA	GCCTCACGGT NGTGCTGTTN	GGTGTCTTTC GCTATTTTNC
HSOAD55R HNEDU15X HSLAH84R HLTBM08R	TACCAGGTGG CTNCCTNTTC AAGTTTTAAA	TNTGGTAACC	TCTTAGGAAG	GAAGGATTCT	TAACTGGGAA

LICOADEED	401				450
HSOAD55R HNEDU15X HSLAH84R HLTBM08R	ATAACCCAAA	AAAANNTTAA	AGCTGCCAGC ANGGGTANGN AAATATGGTC	AGGAGCAGGA GNNANANGNG	GGGNNGTTNN
	451			•	500
HSOAD55R HNEDU15X HSLAH84R HLTBM08R	CNNGNNGNNT	TTTNGGNNTA	GCTGTCACCG TNTTNTNNTN CANGGNGAGG	GGGNNNNGTA	AAAATGGGGC
	501				550
HSOAD55R HNEDU15X HSLAH84R			CAACTCCAGT		
HLTBM08R			•••••	• • • • • • • • •	• • • • • • • • • •
	551		•		600
HSOAD55R HNEDU15X HSLAH84R	TGCCGTTCAG		AAACAGTCAC		TTGCAACTGA
HLTBM08R	••••••				
	601				650
HSOAD55R HNEDU15X	TTGCAGACAG		ACTATACAAA		
HSLAH84R HLTBM08R	• • • • • • • • • • • • • • • • • • • •				
	651				700
HSOAD55R HNEDU15X	CCATGGCTTC	TCAGCTTTAA	AAGGGGAAGT	GCCCTAGAAG	AAAAAGAGAA
HSLAH84R HLTBM08R	• • • • • • • • • • • • • • • • • • • •				• • • • • • • • • • • • • • • • • • • •
	701				750
HSOAD55R HNEDU15X			CTGGTTACTT		GGTCAGGTTT
HSLAH84R HLTBM08R					
	751				800
HSOAD55R HNEDU15X			GCCATGGGAC		GAGGAAGAAG
HSLAH84R HLTBM08R		-,		•	

	801				850
HSOAD55R HNEDU15X		TTGGGGATGA			
HSLAH84R HLTBM08R					
TILTBROOK			•••••		000
HS0AD55R	851			<u>\</u>	900
HNEDU15X	TCAAAATATG	CCTGAAACAC	•		TCAGCTGGCA
HSLAH84R		•			
HLTBM08R		••••••	• • • • • • • • • • • • • • • • • • • •	• • • • • • • • • • • • • • • • • • • •	
	901				950
HSOAD55R HNEDU15X	TTGCAAAACT	GGAAGAAGGA	GATGAACTCC	AACTTGCAAT	ACCAAGAGAA
HSLAH84R	• • • • • • • • • • • • • • • • • • • •				
HLTBM08R	• • • • • • • • •	• • • • • • • •	• • • • • • • • • •		
	951,		•		1000
HSOAD55R HNEDU15X		TATCACTGGA		ACATTTTTG	
HSLAH84R					
HLTBM08R			•••••		
	1001	·			1050
HSOAD55R		CCTACTTACA		ACCTATITIC	
HNEDU15X HSLAH84R	ACIGCIGIGA				
HLTBM08R					
	1051				1100
HSOAD55R					
HNEDU15X HSLAH84R		AAGAAGAAAG			
HLTBM08R					
HSOAD55R	1101				
HNEDU15X	AAAAAA				
HSLAH84R					
HLTBM08R	••••				

FIG.4C

Neutrokine- α SV

1		GATG D D	ACT(S	CAC T	AGA E		GG/ E	AGC <i>A</i> Q	AGTO S	R	GCCT L	TAC T	TTO S	CTT(GCC ⁻	TTA. K		AAA R	GAGAA E	A 60 20
61 21				GAA K		GTG C	TGT V	TTC S	CAT I			CACE R			<u>S</u>	GCC(CTG V	TCCGA R	120 40
121 41	<u>S</u> .	TCCA S <u>K</u> D-I		CGG G	AAA K	GCT <u>L</u>	GCT L	GGC A		CAAC T	CTT L	GCT L	GCT L	GGC A	CACT	TGCT L	TGT(S	CTT(GCTGC C	180 60
181 61		ACGG [*]				CTA Y		GGT V	_	CGC A	CCT <u>L</u>	GCA Q	AGG G	GGA D	L_		S	GCCT L	TCCGG R	240 80
241 81	GCAC A E CD - 1		TGCA Q	GGG G	CCA H	CCA H	CGC A	GGA E	GAA K	GCT L	GCC P	AGC A		AGC A	G		Р		AGGCC A	300 100
	GGCC <u>G L</u> CD-III	. E		AGC` A	TCC. P	AGC A	TGT V	CAC T	CGC A	GGG G	ACT L	GAA K	AAT I	CTT F	TGA E	ACC P	ACC P	AGC A	TCCA P	360 120
361 121	GGAG G E				CAG [*] S					AAA N						GGG	TCC P		NAGAA E	420 140
421 141	ACAG T G		TTA Y	CAC/ T	ATT F	TGT V	TCC. P	ATG W	GCT L	TCT(CAG S	F	TAA <u>K</u> - IV	AAG R	GGG G	AAG S	TGC A	CCT L	AGAA E	480 160
	GAAA <u>E K</u> CD-IV	E	AGAA N		4A TA <u>I</u>		GGT(AGA E	,	G	TTA(<u>Y</u> CD - \	F	F	TAT I	ATA Y	TGG G	TCA Q	GGTT V	540 180
541 181	TTAT L Y	ATAC T	D	TAA(<u>K</u> D - V]	T	CTA(Y			GG/ <u>G</u>	АСА ⁻ <u>Н</u>	ΓCΤ <i>i</i> L	AAT I	Q		K	GAA K		CCA H	TGTC V	600 200

FIG.5A

Neutrokine- α SV

601 201	TTTGGGGATGAATTGAGTCTGGTGACTTTGTTTCGATGTATTCAAAATATGCCTGAAACA	660
	CD-VIII CD-VIII	220
661	CTACCCAATAATTCCTGCTATTCAGCTGGCATTGCAAAACTGGAAGAAGGAGATGAACTC	720
221	L P N N <u>S C Y S A G</u> I A K <u>L E E G D E L</u>	240
	CD-IX CD-X	
721	CAACTTGCAATACCAAGAGAAAATGCACAAATATCACTGGATGGA	780
241	Q L A I P R E N A Q I S L D G D V T F F	260
	CD-XI CD-XI	
701		
781 261	GGTGCATTGAAACTGCTGTGACCTACTTACACCATGTCTGTAGCTATTTTCCTCCCTTTC G A L K L L	840
201	CD-XI	266
	·	
841	TCTGTACCTCTAAGAAGAAAGAATCTAACTGAAAATACCAAAAAAAA	900
	AAA 000	
901	AAA 903	

FIG.5B

NEUTROKINE-aSV

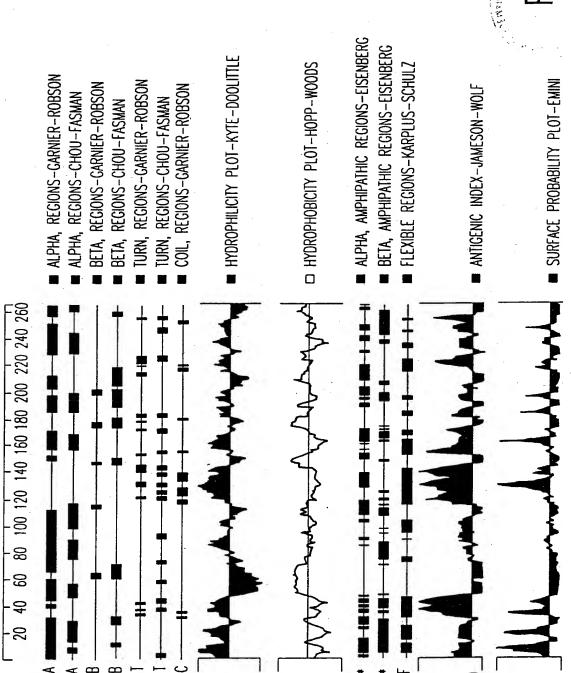


FIG 6

Neutrokine-Alpha M D D S T E R E Q S R L T S C L K K R E E M K L K E C V S I L P R K E S P S V R S

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FIG.7A-1

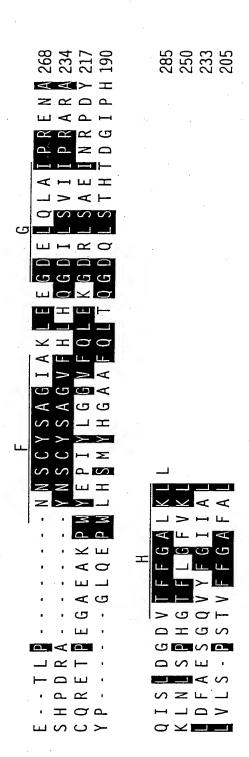
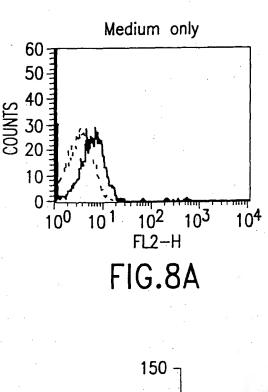
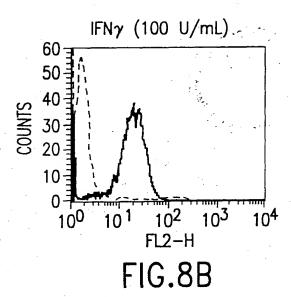


FIG.7A-2

HL-60
HeLa
K-562
MOLT-4
Raji
SW480
Spleen
Lymph Node
Thymus
PBL
Bone Marrow
Fetal liver
Heart
Brain
Placenta S. Muscle Kidney Pancreas

FIG.7B





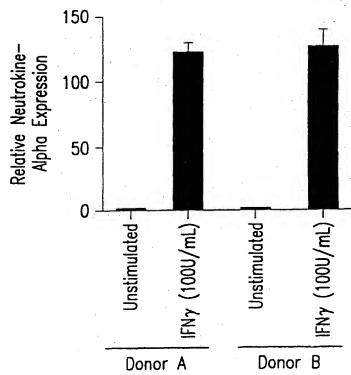
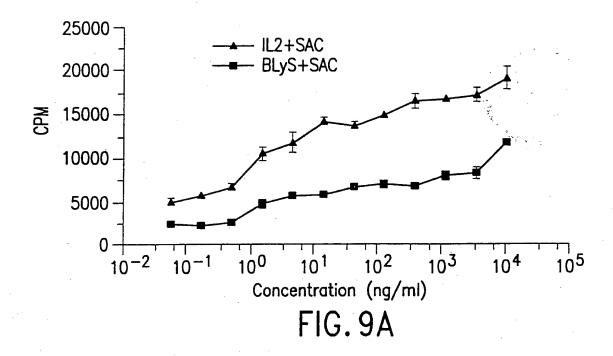
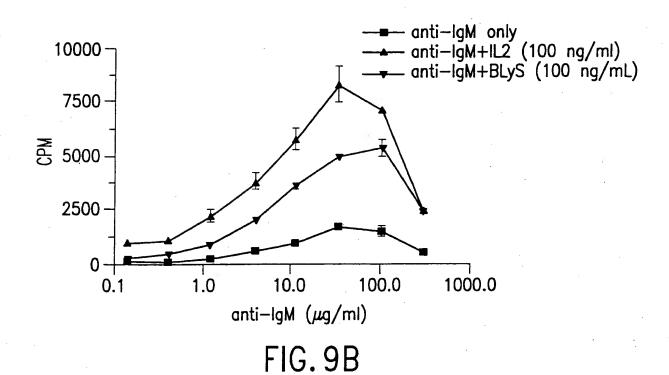


FIG.8C





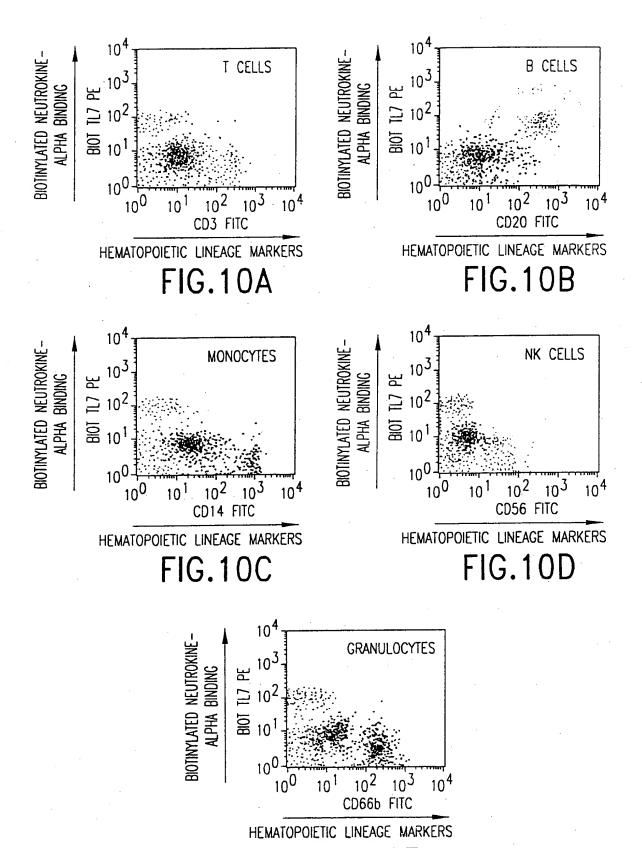
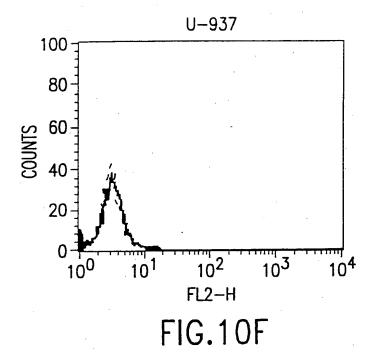
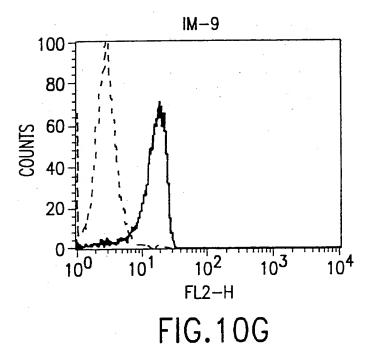


FIG.10E





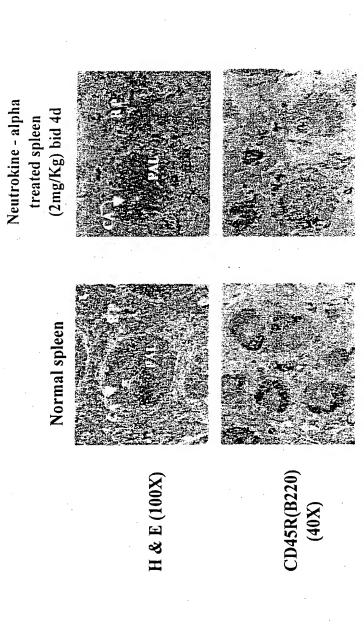
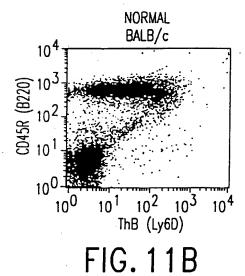


FIG.11A



NEUTROKINE - ALPHA TREATED BALB/c

10⁴

10²

10²

10⁰

10⁰

10¹

10⁰

10¹

10²

10⁰

ThB (Ly6D)

FIG. 11C

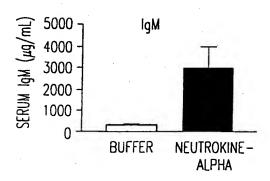


FIG. 11D

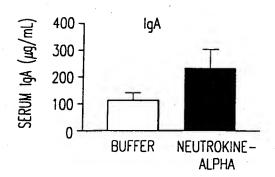


FIG. 11E

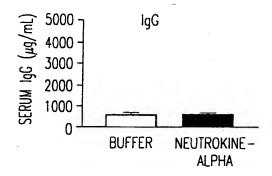


FIG. 11F

Figure 7

a.

```
leutrokine-
ulpha M DDSTEREQSRLTSCLKKREEMKLKECVSILPRKESPSVRS 472
                                                                                                            DELETE PORTION OF
                                                                                                                                   UNE
                                          Transmembrane
                                                                Region
        SKDGKLLAATLLLALLSCCLTVVSFYQVAALQGDLASLRAE
                                                                                                                                      IN
        LQGHHAEKLPAGAGAPKAGLEEAPAVTAGLKIFEPPAPGE G. 123
        NSSQNSRNKRAVQGPEETVTQDCDQLTABSETPTIQKGSYT 164
April HSVLHLVPINATSK-DDSDVT 134
TNF KPVAHVVANPQAEGQ----- 102
                                                                                                                                          10
                                                                KPAAHLIGDPSKQNS---
                                                  LT a
                                                                                                                                  "6" at position
        FVPWELS----FKRGSALEEKENKILVKETGYFFLYGOVE 200
EVMWQPA----LRGGRGLQAQGYGVRIQDAGVYLLYSOVL 170
-LQWLNRRANALLANGVELRD--NQLVVESEGLYLLYSOVL 139
-LLWRANTDRAFLQDGFSLSN--NSLLVPTSGIYFVYSOVV 114
                                                                                                                                   pe black
                                                                                                                                      text on
                                                                                                                                         Shite background
        YTDKTY - - - AMEHLIQRKKVHVFGDELSLVTLFRCLQNMP
FQDVTF - - - FMGQVVSRE - - - - - GQGRQETLFRCLRSMP
FKGQGCP - - - STHVLLTHTISRIAVSQQTKVNLLSAIKSP
FSGKAYSPKAFSSPLYLAHEVQLFSSQXPFHVPLLSSQXNV
        E - T L P - - - - - N N S C Y S A G I A K L E E G D E L Q L A L P R E N A 268 S H P D R A - - - - - Y N S C Y S A G V F H D H O G D I L S V I L P R A R A 234 C Q R E T P E G A E A K P W Y E P I Y L G G V F Q L E K G D R L G A E I N R P D Y 217 Y P - - - - - G L Q E P W L H S M Y H G A A F Q L T O G D Q L S T H T D G I P H 190
        QISLDGDVTFFGALKLL
KLNLSPHGTFLGFVKL
LDFAESGQVYFGIIAL
LVLS-PSTVFFGAFAL
                                                                                                                            285
                                                                                                                            250
                                                                                                                            233
                                                                                                                            205
```

b.

